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A Study of Gestational Trophoblastic Disease at A Tertiary Care Centre

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ABSTRACT

Gestational trophoblastic disease (GTD) defines a heterogeneous group of interrelated lesions that arise from the trophoblastic epithelium of the placenta.

The aim of this study was to know the incidence of the gestational trophoblastic disease and classify them as per WHO classification and to assess the significance of classifying hydatidiform moles into its sub-types.

Cases diagnosed as GTD during a period of seven year from June2007-June2014 were reviewed.

80 cases of GTD were diagnosed in the seven year period. The lesions observed included a majority of Complete and Partial type of Hydatidiform mole, 4 cases of Choriocarcinoma and a single case each of Invasive mole and Placental Site Trophoblastic Tumour (PSTT).

This study concluded that introduction of routine first trimester ultrasound combined with effective follow up programs resulted in near 100% cure rates for patients with molar pregnancies.

KEYWORDS | Gestational trophoblastic disease, hydatidiform mole

Introduction-

Gestational trophoblastic disease (GTD) defines a heterogeneous group of interrelated lesions that arise from the trophoblastic epithelium of the placenta.

The aim of this study was to know the incidence of the gestational trophoblastic disease and classify them as per WHO classification and to assess the significance of classifying hydatidiform moles into its sub-types.

Observations-

80 cases of gestational trophoblastic disease were diagnosed in the seven year period.

Hydatidiform moles formed the majority of the cases of Gestational trophoblastic disease. Incidence of Hydatidiform mole was common in 21 – 25 yrs of age (37.83%) followed by age group 26 – 30 yrs (32.43%). Most of these cases were primiparous (58.11%). 4 cases presented with Choriocarcinoma. Age incidence of Choriocarcinoma was more in 26 – 30 yrs (50%), followed by one case each in 21 – 25 years group and 36 – 40years group. All four cases were primiparous.

A single case of Invasive mole was seen in 38 years old multiparous women (Para 6).

A single case of Placental Site Trophoblastic Tumour was seen in primiparous woman in first trimester. Hydatidiform Mole cases presented most commonly in second trimester.

Although the levels of β HCG were raised in both complete and partial mole, the levels were higher in complete moles than that in partial moles.

There were 74 cases of hydatidiform mole of which 45 (60.81%) were complete mole and 29 (39.1%) were partial mole. Out of 74 cases of Hydatidiform Mole, 16 cases were primigravida, 11 cases had a bad obstetric history in the form of abortion, still-birth, etc. while 47 had a history of prior normal term pregnancy. Out of 4 cases of choriocarcinoma, one had past history of Hydatidiform Mole 1 year back while 3 had history of uneventful antecedent pregnancy. Interval between antecedent pregnancy and choriocarcinoma was 1 month in one case and 1 year in other two cases. Choriocarcinoma metastasized most commonly to the lungs followed by the brain, liver, kidney and abdomen including intestinal tract.

Discussion-

There is a wide variation in incidence reported worldwide which has been attributed to genetic, environmental, and host-related factors. Although several environmental factors such as protein deficiency, malnutrition and low socio-economic status have been proposed as contributing to this geographic and ethnic distribution, definite environmental factors have not been demonstrated.[1]

The incidence of Gestational Trophoblastic Diseases was 1:888 deliveries forming 0.112% and as per live births the incidence was 1:844 live births (0.118%).

This incidence correlated well with Indian studies[2,3,4] and with a study of Iraq[5,6]

The two or three-fold higher incidence of molar pregnancy in the countries of South-East Asia than that of USA or Europe has been reported on the population-based study. [1]

The incidence of Choriocarcinoma of this study [(1:17775 deliveries) or (1:16897 live births)] was also comparable with an Indian and Iraq study.[5,7]

Majority of patients were in the third decade (21-30 yrs) and presented in early second trimester (55.26%) with symptoms of vaginal bleeding and lower abdominal pain. Maternal age has been consistently identified as an important risk factor and extremes of age is a known risk factor [3].

Although with routine first trimester ultrasound a majority of complete molar pregnancies are diagnosed by 8-12 weeks gestation we observed patients of molar pregnancy presenting in second trimester of gestation as this study was conducted in a tertiary care referral center where patients were directed from primary health centres. Although 08 cases were reported in 21 – 24 weeks of gestation, none of them presented with preeclampsia or toxemia.

Majority of patients with advanced molar pregnancy presented with liquefaction of intrauterine clots which led to leak-

age of fluid with the colour and consistency of prune juice. Some undiagnosed patients passed molar vesicles or even miscarried the entire molar tissue. Pre-eclampsia can occur in up to 25% of advanced molar pregnancy whilst it is extremely rare if the molar pregnancy is diagnosed prior to 10—12 weeks. Abdominal and pelvic pain results from enlarged theca lutein cysts of the ovary which are commonly associated with advanced molar pregnancy and are assumed to be linked to the high HCG levels [5].

Similar to other Indian study,[2] most of the histopathological studies on Hydatidiform Mole revealed a higher incidence of Complete Hydatidiform Mole as compared to Partial Hydatidiform Mole. This histopathological distinction between the two types of molar pregnancy and non molar failed pregnancies can be helpful in both determining the likelihood of the relative risk of developing persistent Gestational Trophoblastic Neoplasia and when the diagnosis proves to be a non-molar failed pregnancy, it limits the follow up and restrictions on the timing of future pregnancies [5].

In addition to the histological analysis, a number of techniques have been shown to be useful in aiding the accurate diagnosis of the type of molar pregnancy. Molar ploidy analysis by flow cytometry is useful in distinguishing Partial Hydatidiform mole from Complete Hydatidiform mole, whilst testing for the expression of p57, a maternally imprinted cdk inhibitor, is helpful in distinguishing the androgenetic complete moles where it is negative, from cases of partial mole or non-molar pregnancies which do express this antigen [8].

In the present study, Hydatidiform Mole was more common in primiparous (58.11%) than in nulliparous patients which was similarly seen in various studies[5,3,2]

It should be noted that patients with uterine size 4 weeks larger than date and the presence of theca lutein cyst of >6cm have a 50% risk of persistent disease [7].

Although uterine size 4 weeks greater than date is a classic manifestation of advanced molar pregnancy as a result of the trophoblast hyperplasia and haemorrhage, approximately 15-40% of patients have a 'small-for-dates' uterus [5]. This study revealed 13.5 % cases with uterine size smaller for Gestational age. A majority of 35 cases (47.29%) had uterine size larger than Gestational Age. This finding correlated well with most Indian studies.[2,3,9]

Bad obstetric history was observed in 18% of non-primigravida women History of prior spontaneous miscarriage appears to increase the risk of a molar gestation (both partial and complete hydatidiform mole), with studies demonstrating a two- to three-fold increase in risk of hydatidiform mole in women with prior spontaneous abortion compared to those without a history of prior miscarriage [2,8].

In 2002, the International Federation of Gynecology and Obstetrics established new criteria for the diagnosis of persistent neoplasia after a molar pregnancy.[10] These criteria include serum HCG levels that do not return to the normal range after evacuation, evidence of metastasis, and a pathological diagnosis of Choriocarcinoma, any one of which establishes the diagnosis of persistent neoplasia.

Patients with a complete mole who have markedly elevated HCG levels and an abnormally large uterus before evacuation are categorized as being at high risk for subsequent gestational trophoblastic neoplasia [6].

The reported risk of the development of gestational trophoblastic neoplasia after a partial molar pregnancy ranges from 0 to 11% [11] and after complete hydatidiform mole is 18 – 29%.

In the present study, Hydatidiform mole as an antecedent pregnancy was seen in one out the four cases of choriocarcinoma. All 04 cases showed evidence of metastasis with common involvement of lungs (75%).

All forms of Gestational Trophoblastic Disease produce β HCG which therefore acts as a tumor marker. Serum β HCG levels correlate with disease volume and hence monitoring its levels is used as an accurate biomarker for diagnosis, prognosis and follow up of Gestational Trophoblastic Disease.[10]

In molar gestations, β HCG levels at diagnosis are variable, but most show a markedly elevated HCG titer, which is a useful diagnostic feature. Levels greater than 2 million m IU/ml have been reported. β HCG titers are generally higher in complete than partial moles. Choriocarcinoma, almost invariably, produces very high level of β HCG and a case with a level of 11 million m IU/ml has been reported. In contrast to the high levels in Hydatidiform moles and Choriocarcinoma, β HCG levels are much lower in Placental site trophoblastic tumor and epithelioid trophoblastic tumors. Nevertheless, β HCG levels are very useful in monitoring patients with these tumors. [11]

Hyperglycosylated HCG is now believed to be the marker for malignant Gestational Trophoblastic Neoplasia, and its presence is associated with response to chemotherapy. The pattern of HCG regression and the ratios of HCG components have been reported to be useful. Recently analysis of hyperglycosylated HCG levels and the ratio of the HCG beta component to the total HCG concentration have also been shown to be of potential predictive value, but insufficiently sensitive to base treatment decisions on.[11]

Summary

Gestational Trophoblastic Neoplasia forms a group of rare but almost uniformly curable malignancies using treatments of low toxicity. For the more challenging cases of choriocarcinoma and PSTT presenting with distant disease but without any gynecological symptoms or a recent pregnancy, laboratory measurement of the serum hCG level can be life saving as it will allow the diagnosis to be made and effective treatment to be commenced. To produce the optimal outcome for these patients, optimizing molar pregnancy follow up services and the education to the potential diagnosis of Gestational Trophoblastic Neoplasia in women with bad obstetrics history are the most important factors in ensuring effective patient care.

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